demonstrate 9.4% of patients with positive troponin levels and no CAD had a history of congestive heart failure (CHF) as opposed to 2.7% of troponin-negative and no-CAD patients. A p value is given only for comparison across all four subgroups. No statistical comparison is made for the presence of CHF between the two subgroups of patients without CAD, nor is multivariate analysis available. It is possible that this finding influences the prognosis in this subgroup, without direct relation to the finding of elevated troponin. The finding of elevated B-type natriuretic peptide (BNP) as demonstrated in Table 2 (1) in the troponin-positive, CAD-negative group supports this contention.

In summary, far larger studies with correction for CHF, elevated BNP, and left ventricular function are necessary to truly assess the prognosis of patients with ACS with elevated troponin and nonsignificant CAD.

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Troponin Levels and Acute Coronary Syndrome

We read with interest the recent study by Dokainish et al. (1). Both the aim and the result of the study are challenging; this is because the investigators have suggested significant prognostic evidence for troponin (Tp)-positive patients with acute coronary syndromes (ACS) but without significant coronary artery disease (CAD). As Dokainish et al. (1) suggested in the Study Limitations section, their investigation has disadvantages in being a substudy with a limited number of patients and with a limited number of patients with index event. The main finding of their study—that so-called false-positive Tp results in patients with ACS but no significant angiographic CAD—begets further attention because of a higher event rate by means of a composite end point in these patients. However, this suggestion should be interpreted cautiously—as mentioned in the Study Limitations—because angiography is not a gold standard for accessing atherosclerosis.

Also, because of the study design it should be remembered that all patients were treated by acetylsalicylic acid (ASA), intravenous heparin, and glycoprotein (GP) IIb/IIIa inhibitor. It is well known that patients with an elevated troponin T level and non–ST-segment elevated ACS (NSTE-ACS) have been reported to benefit particularly from antithrombotic drugs such as platelet GP IIb/IIIa antagonists and low-molecular-weight heparin (2). It is reasonable to hypothesize that the elevated troponin T levels in patients with NSTE-ACS indicate the presence of a thrombus at culprit lesions (3). As is known, a culprit lesion responsible for myocardial infarction is <50% in most cases. Thus, CAD or no-CAD classification by coronary angiography must be questioned.

Conversely, baseline creatinine (Cr) level differed between the two groups (Tp−, no-CAD vs. Tp+, no-CAD) (0.93 ± 0.56 mg/dl, 1.46 ± 2.31 mg/dl, respectively). In the original study, chronic renal failure (CRF) was an exclusion factor (serum Cr >2.5 mg/dl) (4), but in this substudy the mean Cr is high, and the standard deviation is also unexpectedly high. What could be the explanation of this high serum Cr in such a study that excludes patients with CRF? It is well established that patients with CRF have higher Tp levels even without any ACS; the difference in Cr levels may be a consequence of inadequate or slow clearance rather than excess production due to ACS in this group of patients.

It must be remembered that this study basically compares no-CAD patients with or without Tp positivity. Hence, two-way comparisons should be applied instead of four-way comparisons for statistical analysis. As a result, regarding the small event rate, the limitations previously mentioned, and our considerations for the effect of GP IIb/IIIa antagonists in borderline lesions and their effect of undiagnosed renal failure, we believe that the conclusion of the study by Dokainish et al. (1) is quite exaggerated.

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REPLY

We thank Drs. Bybee and Rihal for their valuable comments regarding our study (1). The major point of our publication is that patients presenting with symptoms suggestive of acute coronary syndrome (ACS) who are troponin positive on admission without evidence of significant epicardial coronary artery disease (CAD) on angiography have a worse prognosis than do those who are troponin negative without significant epicardial disease. In our discussion we recognized that the mechanisms conferring this adverse prognosis are not known. Notwithstanding that, we agree with the comments of Drs. Bybee and Rihal that transient left ventricular apical ballooning syndrome (TLVABS) should be included as a potential explanation for troponin positivity in some

of our patients, especially women. It is intriguing to note that the underlying mechanism(s) that account for TLVABS remain unknown. Some of the mechanisms, which we suggested in our study, to explain troponin positivity in the absence of significant epicardial coronary disease may be the same ones responsible for TLVABS, namely coronary vasospasm (2), microvascular ischemia (2), acute myocarditis (3), plaque erosions (4), and others such as emotional stress with possible excessive sympathetic stimulation (5).

We would also like to thank Dr. Leibowitz for his interest in our study. We agree with his comments that the number of patients with positive troponin and no significant epicardial coronary disease on angiography is small. Therefore, as we noted in our Study Limitations section that "the results should be interpreted with caution."

To validate the results of our study, we have analyzed the event rate in all patients included in the TACTICS study who were either troponin-T or -I positive on admission, and who underwent coronary angiography either because they were randomized to the invasive arm or randomized to the conservative arm and subsequently underwent coronary angiography. In this analysis, 57 patients were troponin positive without significant epicardial CAD. Of these patients, one died, two had reinfarction, and four were rehospitalized for ACS. Therefore, the composite event rate was 10.5% at six months compared to no events in the group of patients who were troponin negative without significant epicardial disease.

It is worthwhile to mention also that no statistical differences existed in the incidence of congestive heart failure or LV ejection fraction between the group of patients without epicardial coronary disease with or without troponin positivity on admission (2 of 95 patients vs. 3 of 32 patients; p = NS) and (60.5% vs. 58.3%; p = NS), respectively.

In conclusion, large prospective studies are definitely needed to validate these potentially important results, which have a significant impact on patients presenting with ACS.

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